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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	PAPER NUMBER
1656	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,827	HAYASAKA ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/09/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 1-4 are pending and under examination.

Priority

2. This application is a 371 of PCT/JP04/14919 filed on 10/08/2004, which claims foreign priority to JAPAN 2003-351410 filed on 10/09/2003. The priority is awarded to the aforementioned applications.

Drawings

3. Drawings submitted on 04/06/2006 are accepted by examiner.

Information Disclosure Statement

4. The Information Disclosure Statement filed on 11/09/2007 has been received and entered. The references cited on the PTO-1449 Form have been considered by the examiner and a copy is attached to the instant Office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Molina et al.,"*The effects of divalent cations in the presence of phosphate, citrate and*

chloride on the aggregation of soy protein isolate," Food research International, 32 (1999), pages 135-143, (the reference cited on the IDS submitted on 11/09/2007).

Molina et al. teach aggregate dispersions that were obtained from native soy isolates solutions in water, and in 30 mM phosphate at pH=7, with or without 10mM citrate and calcium and magnesium ions. See page 136, right column, second paragraph (instant claims 1, 2, 4).

Molina et al. teach that the study of protein aggregation was performed at room temperature, at approximately 20°C. See page 136, right column, first paragraph, first line (instant claims 1, 2).

Molina et al. teach that citrate effect was studied for an aggregate dispersion of soy proteins where the addition of increasing amounts of sodium citrate lead to a gradual decrease in turbidity, due to its sequestering effect on cations. See page 140, right column, second paragraph (instant claims 1, 2).

Molina et al. teach that the citrate-inhibiting effect on aggregation of proteins or dissociation of aggregates, is higher in the absence of phosphate. See page 140, right column, second paragraph (instant claims 1, 2).

Molina et al. teach that with or without phosphate, the aggregation was totally inhibited when citrate was added at concentrations above 40Mm, thus it was assumed that low citrate concentration of 10mM was sufficient to observe aggregate stability and see the effects of citrate in dissociation of aggregates. See page 140, right column, second paragraph (instant claims 1, 2).

Claims 1 and 2 are included in this rejection because Molina et al. teach stabilization of proteins (i.e. decrease in aggregation of soy proteins) in a citrate buffer, where the proteins are stabilized by suppressing cryoprecipitation (which is an effect of a stabilization, or where the suppressing of cryoprecipitation occurs because of an addition of a citrate to a protein aggregate).

Further, in the preamble of claim 1, Applicants use the phrase that reads: "for stabilizing a protein at low temperature" where the phrase refers to a "purpose" or "intended use" of the method and is thus not a claim limitation. The court stated that the claim preamble must be read in the context of the entire claim. The determination of whether preamble recitations are structural limitations or mere statements of purpose or use "can be resolved only on review of the entirety of the [record] to gain an understanding of what the inventors actually invented and intended to encompass by the claim." *Corning Glass Works,* 868 F.2d at 1257, 9 USPQ2d at 1966. If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997) ("where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation"). See MPEP 2111.02.

Therefore, in the instant case, the phrase "for stabilizing a protein at low temperature" is only stating the purpose or the intended use for the invention, and it is not a claim limitation.

Even though the low temperature is not required in the claims as presented, Molina et al. nevertheless teach that the study was performed at 20°C temperature, which is a low temperature (instant claim 1).

Claim 4 is included in this rejection because the pH was 7, which is in the range of claim 4. Also, it is known in the art that since the citrate has three pKas values the pH of the citrate buffer ranges from 3 to 7, which is in the range of claim 4 that is 5 to 8.

Therefore, the aforementioned claims are anticipated by Molina et al.

Claims 1-2 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Flink (WO 99/37329) (the reference cited on the IDS submitted on 11/09/2007).

Flink teaches isotonic pharmaceutical formulation and a method for the storage of antibodies by using such formulation, comprising an antibody at 0.5 mg/ml to 10 mg/ml and a citrate buffer present at 5 mmol/l to 20 mmol/l, at pH from 5.3 to 7.2. See Abstract, and page 2, lines 5-14 and lines 20-23 (instant claims 1-2 and 4).

Flink teaches that the stabilization preparation was made by addition of a citrate buffer at different concentrations to a humanized antibody. See page 6, lines 8-10 and examples on pages 7 to 9. Further, the best stability was observed at low storage temperature +5°. See page 9, line 8 (instant claims 1-2 and 4).

Flink teaches in claim 15, a process for the preparation of an isotonic pharmaceutical formulation comprising incorporation of an antibody in an isotonic medium wherein the antibody is present at 0.5 mg/ml to 10 mg/ml, and wherein the citrate buffer is present at 5 mmol/l to 20 mmol/l at pH from 5.3 to 7.2. (Therefore, Flink teaches a method of preparation of stabilized antibody, such as IgM, instant claims 1-2 and 4).

Also, in claim 21, Flink teaches a method for improving the storage of antibodies using the citrate buffer; and claims 22 and 23 teach a method where the antibody formulation is stored at temperature between 4°C to 10°C. (instant claims 1-2 and 4, where the temperature is low).

Therefore, the aforementioned claims are anticipated, because Flink teaches a method for stabilizing antibodies, which are proteins, at low temperature, and thus suppressing cryoprecipitation, where the citric acid is used at pH from 5.3 to 7.2. Above all, Flink teaches that the antibody can be stabilized only by a citrate buffer at physiological pH, and therefore, the aforementioned claims are anticipated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Flink (WO 99/37329) (the reference cited on the IDS submitted on 11/09/2007).

The teachings of Flink are disclosed above where he does not teach a protein that is IgM.

Flink teaches that his antibody preparations and the methods for storage (i.e. stabilization of proteins during storage) are suitable for any antibody or any antibody fragment. See page 3, line 13. (instant claim 3 where the antibody is IgM).

Therefore, it would have been obvious to one skilled in the art at the time the invention was made to design a method of stabilizing IgM protein at low temperature wherein the method comprises a citric acid buffer because Flink teaches antibody preparations and the methods for storage for any antibody or any antibody fragment that would encompass IgM protein. One would be motivated to use such a preparation for stabilizing IgM because Flink teaches that such methods are successful in storing any antibody. Moreover, there is a reasonable expectation of success that Flink's protein will be functional with any antibody based on the high level of skill in the art. Therefore, the invention is *prima facie* obvious.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone

number for the organization where this application or proceeding is assigned is 571-272-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

/Kathleen Kerr Bragdon/

Supervisory Patent Examiner, Art Unit 1656